SUBSTITUTE SPECIFICATION – CLEAN VERSION

CLAIMS

1. A disease model animal expressing megsin gene, a gene encoding the receptor for advanced glycation end-products, and an inducible nitric oxide synthase gene, wherein the model animal comprises a nonhuman mammal.

2. The disease model animal of claim 1 introduced with megsin gene, a gene encoding the receptor for advanced glycation end-products, and an inducible nitric oxide synthase gene.

3. The disease model animal of claim 1 or 2, which exhibits at least one phenotype selected from the following phenotypes (a) to (f):

(a) increase in kidney-to-body weight ratio;

(b) increase in urine albumin level;

(c) increase in blood triglyceride level;

(d) underweight (hypogenesis);

(e) hyperglycemia;

(f) hypoinsulinemia; and

(g) increase in urine 8-OHdG level.

4. The disease model animal of claim 1 or 2, which exhibits in mesangial matrix at least one of the following findings:

(a) expansion of mesangial matrix;

(b) enhancement of immunoglobulin and/or complement accumulation; and

(c) increases of collagen, laminin, and/or fibronectin.

5. The disease model animal of claim 1 or 2, which exhibits in tubular interstitium the phenotypes of:

(a) fibrosis; and/or

(b) infiltration of inflammatory cells.

6. The disease model animal of any one of claims 1 to 5, wherein the megsin gene, the gene encoding the receptor for advanced glycation end-products, and the inducible nitric oxide synthase gene are derived from human.

7. The disease model animal of any one of claims 1 to 6, wherein the disease is diabetic nephropathy.

8. A method for creating a disease model animal, comprising the step of introducing megsin gene, a gene encoding the receptor for advanced glycation end-products, and an inducible nitric oxide synthase gene into a fertilized egg of a nonhuman mammal, wherein the disease model animal comprises a nonhuman mammal in which expressions of the megsin gene, the gene encoding the receptor for advanced glycation end-products, and the inducible nitric oxide synthase gene are enhanced.

9. A method for evaluating the therapeutic effect of a test compound on kidney function disorder, which comprises the steps of:

(1) administering a test compound to the disease model animal of any one of claims 1 to 7; and

(2) detecting the relieving effect on the kidney function disorder of the disease model animal administered with the test compound.

10. A method for evaluating the therapeutic effect of a test compound on kidney function disorder, which comprises the steps of:

(1) administering a test compound to the disease model animal of any one of claims 1 to 7; and

(2) measuring at least any one of kidney-to-body weight ratio, urine albumin level, blood triglyceride level, and urine 8-OHdG level in the disease model animal after administration of the test compound.

11. A method for evaluating the therapeutic effect of a test compound on kidney function disorder, which comprises the steps of:

(1) administering a test compound to the disease model animal of any one of claims 1 to 7; and

(2) determining whether the mesangial matrix of the disease model animal is altered or whether the alteration is reduced after administration of the test compound.

12. The method of claim 11, wherein the alteration of the mesangial matrix is at least one of:

(a) expansion of mesangial matrix;

(b) enhancement of immunoglobulin and/or complement accumulation; and

(c) increases of collagen, laminin, and/or fibronectin.

13. A method for evaluating the therapeutic effect of a test compound on kidney function disorder, which comprises the steps of:

(1) administering a test compound to the disease model animal of any one of claims 1 to 7; and

(2) determining whether the tubular interstitium of the disease model animal is altered or

whether the alteration is reduced after administration of the test compound.

14. The method of claim 13, wherein the alteration of the tubular interstitium is:
(a) fibrosis; and/or
(b) infiltration of inflammatory cells.

15. The method of any one of claims 9 to 14, wherein the kidney function disorder is a kidney function disorder that accompanies hyperglycemia.

16. A method evaluating the therapeutic effect of a test compound on hyperglycemia, which comprises the steps of:
(1) administering a test compound to the disease model animal of any one of claims 1 to 7; and
(2) determining the glucose or/insulin level in the disease model animal after administration of the test compound.